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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,941	07/25/2003	Pamela T. Manning	01073/1 US	3233

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Pharmacia Corporation
Corporate Patent Department
P.O. Box 1027
Chesterfield, MO 63006

EXAMINER

SPIVACK, PHYLLIS G

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 02/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/626,941	Applicant(s) MANNING ET AL.	
	Examiner Phyllis G. Spivack	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 September 1004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11-22-04</u> . | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1614

Applicants' Amendment and response to an Election Requirement filed September 13, 2004 are acknowledged. Applicants have elected nine named compounds of instant Formula II.

An Information Disclosure Statement filed November 22, 2004 is further acknowledged and has been reviewed.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-43 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 91-108 of U.S. Patent No. 6,586,474. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed compounds are encompassed in the patent for use in the treatment of inflammation-related disorders. Inflammatory bowel disease, ulcerative colitis, gastritis and ileitis, *inter alia*, are inflammation-related disorders.

Claims 1-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

Art Unit: 1614

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to the treatment of any condition or disease of the gastrointestinal tract involving an overproduction of nitric oxide by inducible nitric oxide synthase (iNOS). The specification provides support for the administration of various nitric oxide synthase inhibitors that decrease the rise in plasma nitrite/nitrate levels, an indicator of the production of nitric oxide induced by endotoxin in Table I. Table II demonstrates an ability of various compounds to inhibit inducible nitric oxide synthase activity *in vivo*.

Attention is directed to In re Wands, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

- 1) the quantity of experimentation necessary
- 2) the amount of direction or guidance provided
- 3) the presence or absence of working examples
- 4) the nature of the invention
- 5) the state of the art
- 6) the relative skill of those in the art
- 7) the predictability of the art and
- 8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

Art Unit: 1614

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to treatment of any condition or disease of the gastrointestinal tract involving an overproduction of nitric oxide by inducible nitric oxide synthase.

The relative skill of those in the art is generally that of a Ph.D. or M.D. with expertise in the field of gastroenterology.

Each particular gastrointestinal disease or condition has its own specific characteristics and etiology. The unpredictability observed with single agent therapy is compounded when a combination of agents is employed, as required by claims 14-43. The broad recitation "treating a condition or disease of the gastrointestinal tract involving an overproduction of nitric oxide by inducible nitric oxide synthase" is inclusive of many conditions that presently have no established successful therapies.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad and inclusive of any disease or condition of the gastrointestinal tract.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to a demonstration of a decrease in the rise of plasma nitrite/nitrate levels and inhibition of nitric oxide synthase activity.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to a nexus between a condition or disease of the gastrointestinal tract involving an overproduction of nitric oxide by inducible nitric oxide synthase and the treatment of a specific gastrointestinal disease. The skilled artisan would expect the interaction of a particular compound or combination of drugs in the treatment of a particular disease state to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. The instant specification sets forth no such understanding or any criteria for extrapolating beyond the inhibition of iNOS. There is no support for any treatment modality comprising the administration of one of the claimed compounds of claims 1 or 22 with an antimicrobial compound and/or an antisecretory compound. Absent reasonable *a priori* expectations of success for using a particular chemotherapeutic agent or combination of agents to treat any particular gastrointestinal disease, one skilled in the gastrointestinal art would have to test extensively the claimed compounds, optionally in combination with an antimicrobial compound and/or an antisecretory compound, in numerous gastrointestinal pathological states to discover in which particular condition efficacy is shown. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

Art Unit: 1614

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached Monday to Friday from 10:30 AM to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Chris Low, can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Phyllis G. Spivack
Primary Examiner
Art Unit 1614
PHYLLIS SPIVACK
PRIMARY EXAMINER

February 21, 2005